Theories of Disease Causation: An Overview

Dharmashree Satyarup[1], Manish Kumar[2], Radha Prasanna Dalai[3], Sharmistha Mohanty[4], Karishma R. Rathor[5]

[1]Professor, Department of Public Health Dentistry, Institute of Dental Sciences, Siksha 'O' Anusandhan (Deemed to be University), Bhubaneswar, Odisha, India, [2]Professor & Head, Department of Public Health Dentistry, GITAM Dental College and Hospital, Visakhapatnam, Andhra Pradesh, India, [3]Senior Lecturer, [4]Postgraduate Student, [5]Tutor, Department of Public Health Dentistry, Institute of Dental Sciences, Siksha 'O' Anusandhan (Deemed to be University), Bhubaneswar, Odisha, India

Abstract

Disease is an important entity in healthcare. In-depth understanding of disease causation aids in planning prevention and steps to tackle the disease in a population. The outlook regarding disease causation has changed considerably with time and advancements in science. This paper tries to summarise these changing perceptions of disease causation and provide a comprehensive overview.

Keywords: *Disease Causation; Theories; Models.*

Introduction

Disease is usually considered the opposite of health, a deviation from the normal function. Webster defines disease as "a condition in which body health is impaired, a departure from a state of health, and alteration of the human body interrupting the performance of vital functions". However, from an ecological view, disease is defined as "a maladjustment of the human organism to the environment".[1]

The key to finding remedies for the cure of diseases, necessitates an understanding of the cause of the disease. But our perception of disease causation has undergone a vast alteration with the ever changing advancement of science and its contribution to health. Our explanation of disease causation is based on these:

Corresponding Author:
Dharmashree Satyarup
Professor, Department of Public Health Dentistry, Institute of Dental Sciences, Siksha 'O' Anusandhan (Deemed to be University), Bhubaneswar, Odisha, India
e-mail: dharmashree_s@yahoo.com

Theories of disease causation:

i. Theories of the pre-modern era
ii. Germ theory of disease
iii. Biomedical model
iv. Epidemiological triad
v. Dever's epidemiological model
vi. Theory of multifactorial causation
vii. Web of Causation
viii. Wheel of disease causation
ix. Other theories
    - Lazaru's theories of stress response
    - Wolf's theory of stress, organ maladaptation and disease
    - Holmes and Rahe's theory of life change and the onset of illness

i. Theories of the pre-modern era: These theories were in play before the existence of microorganisms was established, till the end of the 18th century.

a. The demonic theory: According to this theory, the disease is a result of being possessed by demons, or evil spirits. Hence the sick person

was subjected to sorcery to rid the body of the evil occupant.

b. **The punitive theory:** For a long time,the disease has been thought to be caused as a punishment for any bad deed done, as an outcome of the outrage of Gods. Hence the diseased individual is to appease the deity to rid himself of the disease.

c. **The miasmatic theory:** It is the notion of bad air. Breathing in certain areas was proposed to cause disease, such as air around swamps, marshes and air at night times was thought to cause an array of diseases.

d. **Theory of four humors:** It proposes that the body is constituent of four humor; blood, phlegm, yellow bile and black bile. Any imbalance in these resulted in disease. Blood-letting was considered the most common method of treating disease.[2]

The Ayurveda believes that the imbalance of the three Doshas (tridosha) is the reason behind disease causation. While the Chinese medicine considers a discrepancy between the male (yang) and female (yin) principle resulting in disease.[1]

ii. **Germ theory of disease:** The demonstration of bacterial presence in the air by Louis Pasteur and Anthrax is caused by bacteria by the turn of the 18th century caused a drastic shift in the understanding of disease causation. Thus, focus from empirical causes such as bad air and wrath of God was altered to scientifically plausible causes like the presence of specific microorganisms.

The germ theory implies the causal effect is one to one, i.e. a single microorganism is the culprit behind a specific disease. Eg. Mycobacterium tuberculosis bacteria and the occurrence of tuberculosis. But that seldom is the case, as many diseases cannot be explained by this one to one causal relation but in reality, an interaction of various other contributory factors.[3]

iii. **Biomedical Model:** This envisions the healthy human body as an efficiently functioning machinery, and any resulting aberration as malfunction of the component organs. Eg. Hypothyroidism caused by improper functioning of the thyroid gland.

But the human body seldom functions independently of its surrounding environment. This theory overlooks the complex and summative role of psychological and social attributes.[4]

iv. **Epidemiological triad:** It proposes the disease is an outcome of imbalance of interactions between three essential components, Host, Agent, and Environment. Disease is caused when a susceptible host is exposed to the causative agent, in a compatible environment.

It's a broader concept and overcomes the limitations of germ theory. Intercepting any of the three links provides a means of halting the disease process, thereby highlighting areas for focus preventive efforts.[5,6]

v. **Dever's epidemiological model:** This model highlights the interplay of four factors namely: Human biology, Lifestyle, Environment and Health system. All of which can have a positive or a negative effect.

Human biology includes genetics along with complex physiological systems, factors that are related to maturation and aging. While, lifestyle factors include daily habits, customs, and traditions; environmental factors are all the living and non-living factors that surround us. Health care system is comprised of accessibility and availability of health services.[7]

This model is used to explain those diseases where, rather than a causative organism, harmful living conditions and lifestyle are to be blamed.

vi. **Multifactorial causation:** Pettenkofer proposed that disease is a result of many factors as opposed to germ theory where the idea of a single cause was used. Improvements in public health and medicine brought about a decline in communicable diseases. But other noncommunicable ailments were on a rise which could not be explained based on the germ theory of disease. Hence single cause was deemed to be oversimplifying etiology of a disease where factors such as social, cultural, genetics, and economic factors were overlooked. Also having multiple causes for a disease meant numerous method of preventing that disease. But it was essential to prioritize the sequence of modification of the causal factors to tackle the disease causation.[1,8]

vi. **Web of causation:** Was proposed by MacMahon, Pugh, and Ipsen (1960), who argued that multiple factors causing a disease cannot be explained using a linear causal relation as, there are complex

precursors to each causal component in the chain that have their respective complex interactions that overlap each other. Hence giving the metaphorical appearance of a complicated ***web of interactions*** rather than a linear causal relation.

This web of causation gives each component equal prominence in recognizing determinants and helps in planning interventions. It integrates social factors to biomedical etiological factors.[9]

vi. **Wheel of disease causation:** This was proposed by Mausner and Kramer in 1985. It eliminates the agent as a sole cause of disease, but emphasizes the complex interaction of physical, biological, and social environments. It also introduces genetics into the mix. The outer circumference is divided between environmental factors comprising of social, biological, and physical factors. The core depicts the genetic component.[6,10,11,12] (Figure 1).

Rothman's Component Causes and Causal Pies Model: It proposes that the causation of disease is by a collection of factors, which are represented by a pie.

This model discriminates the causal factors into ***Sufficient and Necessary causal factors.***

Sufficient cause: is a set of minimum conditions, events, or factors that are required to produce a given outcome. These factors that form the ***sufficient cause*** are called **component causes**. A disease can have more than one sufficient cause.[6]

Necessary cause: is a causal factor whose presence is imperative for the emergence of the effect. If the disease cannot occur without the factor being present then the causative is termed as ***"Necessary".***A component that appears in every pie or pathway is a necessary cause.

So, in figure 2, component cause"A" is present in all pies making it a necessary cause.

The disease can be controlled by removing one component from the pies or the removing the factor that is common to all pies.

Eg: Mycobacterium Tuberculosis bacteria is ***necessary*** to cause tuberculosis but cannot cause the disease in isolation, i.e. is not ***sufficient*** to cause the disease. A host of other factors are required such as impaired nutrition or immunity which can be deemed ***sufficient cause***.

Postulates of Disease Causation: Postulates explaining the process of disease causation have been given by Henle and Koch in 1877 and then by Hill and Evans in 1965. Though our perception about disease causation has changed greatly due to advancements in the field of science, these postulates still hold with some modifications.[13]

a. **Henle-Koch's Postulates:** Postulates were formulated by Robert Koch and Friedrich Loeffler. These postulates helped the germ theory of disease gain popularity over other theories in the 1800s. Certain sets of criteria are to be met before a particular infectious disease agent can be accepted as a cause for a disease.

- The microorganism must be found in abundance in the subject suffering from the disease, but should not be found in healthy subjects.
- The causal microorganism should be isolated from the diseased subject and be grown in pure culture.
- The cultured microorganism thus grown should cause disease when introduced into a healthy organism.
- The microorganism must then be re-isolated from the inoculated, diseased experimental host subjects and cultured and identified as the original causative agent.[14]

However, Koch's postulates can't be applied in all scenarios.[15] As in instances of asymptomatic carriers of diseases such as typhoid and cholera or where two or more microorganisms cause disease. Additionally, some symptoms can be brought about by multiple microorganisms.

b. **Hill-Evans Postulates:** Austin Bradford Hill in 1965 proposed criteria for assessing evidence of causation. These supersede Henle-Koch postulates and considered extensions of Mill's Method of inductive inference (mentioned later). Each criterion contributes to the strength of the causal relationship between a factor and disease.[16]

- **Strength:** Stronger the association between the factor and the disease, more likely it is the causative agent.
- **Consistency:** Consistent observations seen in different scenarios and across different populations strengthens the likelihood of the

causal effect.

- **Specificity:** More specific an association between a factor and an effect, greater the probability of the effect.
- **Temporality:** Exposure to the cause should precede the effect.
- **Biological gradient:** Greater exposure should cause a greater incidence of disease. The strength of causality is reinforced when lesser exposure decreases incidence.
- **Plausibility:** A valid scientific explanation of the causal relationship, though limited by current knowledge is essential.
- **Coherence:** The findings should be coherent with the causal argument.
- **Experimental evidence:** When a feasible causal relationship should be demonstrated.
- **Analogy:** Similar effects should be caused by similar factors.[17]

Another method of inferring causal relation is based on Mill's Eliminative Method of Induction. John Stuart Mill put forth five method of experimental reasoning in his paper System of Logic in 1843. If a specific effect (E) is to be investigated to be caused by the presence of certain factors then the following method are used to reason.[18]

1. Method of agreement: looks for factors present in all circumstances where (E) occurs.
2. Method of difference: advises to look out factors that are present when (E) occurs and the factors that are absent when (E) doesn't occur.
3. Joint method: combining the method of agreement and difference, reinforces the causal relationship.
4. Method of residues: if a range of factors are believed to cause a range of effects, with exception of one factor let's say 'C', and there is an effect that cannot be explained by all the other factors, then we could infer that Factor 'C' is the cause for that effect.
5. Method of concomitant variations: If reducing of a factor causes a reduction in the effect and increasing a factor increases the effect, then a causal relationship between the factor and the effect can be established.[19]

Hence, having a clear picture about the causal mechanism of disease, aids in understanding the disease process, its course and treatment planning. Proper knowledge of disease causation also helps in planning epidemiological studies, adjusting for confounding factors, and ensuring a competent method of research.

Conflict of Interests: None

Ethical Permission: Approved

Funding: Nil

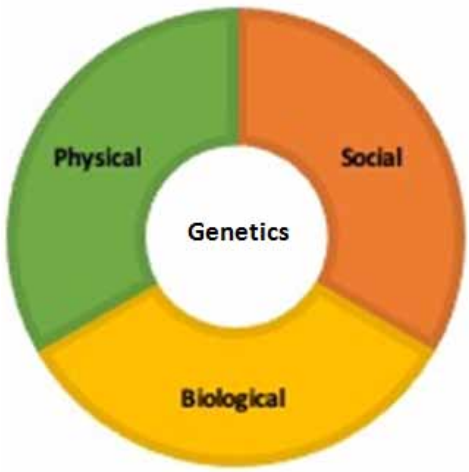

Figure 1. Epidemiological Wheel

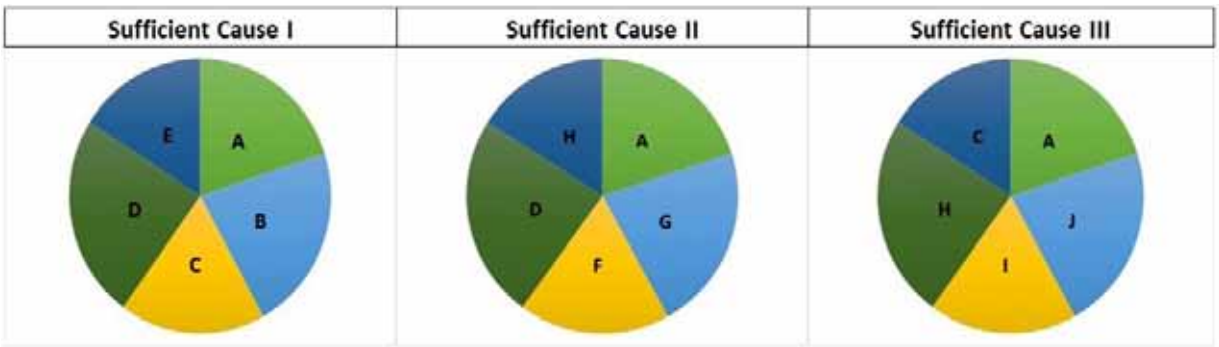

Figure 2. Rothman's Causal Pies

References

1. K. Park. Park's textbook of preventive and social medicine. 21st Edition. Banarsidas Bhanot Publishers.
2. LW Freezer. Theories concerning the causation of disease. Am J Public Health 1921;11(10):908-912.
3. https://www.sciencedirect.com/topics/immunology-and-microbiology/germ-theory-of-disease. Last accessed on 28.03.2020.
4. Alfred S Evans. Causation and disease. A chronological journey. Plenum Medical Book Company.
5. https://www.open.edu/openlearn/health-sports-psychology/health/epidemiology-introduction/content-section-3.1. Accessed on 28.03.2020.
6. https://www.cdc.gov/csels/dsepd/ss1978/lesson1/section8.html. Last accessed on 28.03.2020.
7. GE Alan Dever. An epidemiological model for health policy analysis. Social Indicators Research 1976; 2:453-466.
8. GB Gori. Epidemiology and the concept of causation in multifactorial diseases. Regul Toxicol Pharmacol 1989;9(3):263-272.
9. Krieger N. Epidemiology and web of causation: Has anyone seen the spider? Soc Sci Med 1994;39(7):887-903.
10. https://studymoose.com/the-wheel-of-causation-essay "The wheel of causation." Study Moose, Apr 24, 2016. Accessed March 28, 2020.
11. Maarten Wensink, Rudi GJ Westendorp, and Annette Baudisch. The causal pie model: An epidemiological method applied to evolutionary biology and ecology. Ecology and Evolution. 2014. (4) 10.1002/ece3.1074.
12. Gerald McGwin. Causation in epidemiology. Am J Opthal 2010;150(5):599-601.
13. Alfred S Evans. Causation and disease: the Henle-Koch postulates revisited. Yale J Biol Med 1976;49(2):175-95.
14. TJJ. Inglis. Principia aetiologica: taking causality beyond Koch's postulates. Journal of Medical Microbiology 2007;56(11):1419-1422.
15. AL. Byrd and JA. Segre. Adapting Koch's postulates. Science 2016; 351(6270):224-226.
16. R. Reekum, DL Streiner, and DK Conn. Applying Bradford Hill's criteria for causation to neuropsychiatry: Challenges and opportunities. J Neuropsychiatry Clin Neurosci 2001; 13(3):318-325.
17. Hill AB. The environment and disease: association or causation? Proc R Soc Med 1965;58:293-300.
18. https://www.britannica.com/topic/Mills-method. Accessed on 28.03.2020.
19. S Hollander and S Peart. John Stuart Mill's method in principle and practice: A review of the evidence. Journal of the History of Economic Thought 1999;21(4):369-397.